WHAT IS CLAIMED IS:

1. A method for screening for the bioactivity of a candidate compound toward a group of related target proteins in a proteomic mixture of proteins from a cell, employing at least one probe, each probe characterized by comprising a reactive functionality group specific for said group of target proteins and a ligand and said probe, said method comprising:

combining at least one probe with an untreated portion of said mixture and with a portion inactivated with a non-covalent agent under conditions for reaction with said target proteins;

sequestering proteins conjugated with said at least one probe from each of said mixtures;

determining the proteins that are sequestered; and

comparing the amount of each of the proteins sequestered from the untreated portion and the inactivated portion as indicative of the bioactivity of said candidate compound with said target proteins.

2. A method according to Claim 1, wherein said ligand has a reciprocal receptor and said sequestering is by binding said ligand to said reciprocal receptor bound to a support.

3. A method according to Claim 1, wherein said ligand is detectable as a result of an electromagnetic signal.

4. A method according to Claim 1, wherein said probe is of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group, which is the same in each of the members of the library;

F is a functional group reactive at an active site of a target enzyme, and is the same reactive functionality in each of the members of the library; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L.

5. A method according to Claim 4, wherein F is a sulphonyl group and R is other than H and bonded to F.

6. A method according to Claim 4, wherein F is a fluorophosphonyl or fluorophosphoryl group.

7. A method according to Claim 1, wherein at least one of L and X comprise at least one isotope in unnatural amount, and including the additional step of:

releasing at least a portion of said probe from said conjugate and identifying said portion by means of isotopic difference.

8. A method for screening for the bioactivity of a candidate compound toward a group of related target enzymes in a proteomic mixture of proteins from a cell, employing at least one probe, each probe of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor and/or providing a detectable signal;

L is an aliphatic linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said enzymes;

the * intends that R is a part of F or L;

said method comprising:

combining at least one probe with an untreated portion of said mixture and with a portion inactivated with a non-covalent agent under conditions for reaction with said target proteins;

sequestering proteins conjugated with said at least one probe from each of said mixtures;

determining the proteins that are sequestered; and

comparing the amount of each of the proteins sequestered from the untreated portion and the inactivated portion as indicative of the bioactivity of said candidate compound with said target proteins.

9. A method according to Claim 8, wherein F is a sulphonyl group and R is other than H and bonded to F.

10. A method according to Claim 8, wherein F is a fluorophosphonyl or fluorophosphoryl group.

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11. A method for determining in a proteomic mixture the presence of active target members of a group of related proteins, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining said proteomic mixture in wild-type form with a probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;

combining said proteomic mixture after non-specific deactivation with said probe under said same conditions;

determining the presence of target members conjugated with said probe in said proteomic mixtures in active and inactive form;

whereby when said target members are conjugated to target members in said proteomic mixture in active form and in less amount in inactive form, the presence of active members is determined.

12. A method according to Claim 11, comprising the additional step of characterizing said target members conjugated with said probe in active form and in less amount in inactive form.

13. A method according to Claim 12, wherein said characterizing comprises degrading said target member and determining the resulting fractions by mass spectrometry.

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14. A method according to Claim 11, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

15. A method according to Claim 11, wherein said probe comprises a detectable label.

16. A method according to Claim 11, wherein said proteomic mixture is in an intact cell.

17. A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining each of said proteomic mixtures in wild-type form with a probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;

determining the presence of target members conjugated with said probe in said proteomic mixtures;

analyzing for the presence of target members conjugated with said probe using simultaneous individual capillary electrokinetic analysis or capillary HPLC;

whereby when said target members are conjugated to target members in said proteomic mixtures, the presence of active target members is determined.

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18. A method according to Claim 17 including the additional steps of:

inactivating a portion of said protemic mixture;

combining said inactivated proteomic mixture with said probe under conditions for conjugation;

analyzing for the presence of target members conjugated with said probe in said inactivated proteomic mixture; and

rejecting conjugates from said wild-type proteomic mixture in less amount than the amount of conjugate from said inactivated mixture.

19. A method for determining in a proteomic mixture the presence of active target members of a group of related enzymes, said related enzymes related in having a common functionality for conjugation at an active site, said method comprising:

combining said proteomic mixture in wild-type form with a probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;

combining said proteomic mixture after non-specific deactivation with said probe under said same conditions;

determining the presence of target members conjugated with said probe in said proteomic mixtures in active and inactive form;

whereby when said probe is conjugated to at least one target member in said proteomic mixture in active form and in lesser amount in inactive form, the presence of active members is determined.

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20. A method according to Claim 19, wherein said probe comprises a ligand and said determining is by binding said ligand in a conjugate to a support and isolating said conjugate.

21. A method according to Claim 19, wherein said reactive functionality is a fluorophosphonate or fluorophosphoroate and said enzymes are serine hydrolases.

22. A method according to Claim 19, wherein related enzymes are cysteine hydrolases and said active functionality is an α-haloketone.

23. A method according to Claim 19, wherein related enzymes are enzymes comprising at least one of cysteine, histidine, aspartate and glutamate at said active site and said active functionality is sulfonate ester or epoxide.

24. A method according to Claim 19, wherein related enzymes are aldehyde dehydrogenases and said active functionality is a sulfonate ester.

25. A method according to Claim 19, wherein related enzymes are metalloenzymes and said active functionality is α-halohydroxamic acid.

26. A method according to Claim 19, wherein related enzymes are redox enzymes and said active functionality is an alkyne.

27. A system for identifying active target proteins in a related group of proteins in a sample, using at least one activity-based probe ("ABP") binding to a plurality of members of said proteins, said system comprising:

an ABP of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality for adding a ligand;

L is a linking group, which is the same in each of the members of the library;

F is a functional group reactive at an active site of a target enzyme, and is the same reactive functionality in each of the members of the library; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L;

a sample suspected of containing at least one of said target proteins;

a programmed data processor for receiving and transmitting values, comprising a program for evaluating results from the combining of said at least one ABP and said sample resulting in the formation of conjugates with any of said active target proteins present in said sample to determine the presence of each of said active target proteins in said sample, and providing a profile of the binding of each of said ABPs with said target proteins;

employing a method for obtaining said results, said method comprising:

combining under binding conditions said ABPs and said sample, whereby said ABPs bind to said active target proteins in relation to the on rates of said ABPs with said target proteins;

combining under binding conditions said ABPs and an inactivated sample resulting in the formation of conjugates with any of said inactivated target proteins present in said

sample to determine the presence of each of said inactivated target proteins in said sample, and providing a profile of the binding of each of said ABPs with said inactivated target proteins

determining the amount of conjugate of each ABP for each active target protein and each inactive protein as the results for said data processor;

feeding the results to said data processor; and

transmitting the values for the profile of the binding of said active target proteins as compared to the inactive target proteins.

28. A system for determining the status of a biological system in relation to the presence of members of at least one related group of active proteins, employing the results from combining an ABP of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality for adding a ligand;

L is a linking group, which is the same in each of the members of the library;

F is a functional group reactive at an active site of a target enzyme, and is the same reactive functionality in each of the members of the library; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L; and

a sample suspected of containing at least one of said target proteins;

to produce conjugates of said ABP with said target proteins in varying amounts in relation to the amount of each of said target active proteins;

said system comprising:

a programmed data processor comprising a program for producing a profile of the amount of each conjugate and/or the relative abundance of each conjugate from said results; and

comparing said profile with at least one profile related to a known status of said biological system.

29. A system according to Claim 28, wherein said biological status is an infectious disease.

30. A system according to Claim 28, wherein said biological status is a response to a therapeutic agent.

31. A system according to Claim 28, wherein said biological status is a response to a candidate drug.

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